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EXAMINER	
WEDDINGTON, KEVIN E	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/554,974	TAKAGI ET AL.	
	Examiner	Art Unit	
	Kevin E. Weddington	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 July 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13-31* is/are pending in the application.

4a) Of the above claim(s) *14,19-24,26,29 and 30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13,15-18,25,27,28 and 31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3-2-06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Claims 13-31 are presented for examination.

Applicants' preliminary amendments filed October 28, 2005 and March 2, 2006; and the information disclosure statement filed March 2, 2006 have been received and entered.

Applicants' election filed July 25, 2007 in response to the restriction requirement of June 27, 2007 has been received and entered. The applicants elected the invention described in claims 13, 15-18, 25, 27, 28 and 31 (Group I) without traverse.

Claims 14, 19-24, 26, 29 and 30 are withdrawn from consideration as being drawn to the non-elected invention (37 CFR 1.142(b)).

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent

either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 13, 15-18, 25, 27 and 28 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 41, 43-47, 57, 59 and 60 of copending Application No. 10/555,076. Although the conflicting claims are not identical, they are not patentably distinct from each other because the copending application teaches a method for enhancement of adiponectin production in a warm-blooded animal with an effective amount of one or more HMH-CoA reductase inhibitor(s); and the present application teaches a method for enhancing glucose uptake into warm-blooded animal cells with an effective amount of one or more HMG-CoA reductase inhibitor(s). Note that adiponectin is a protein hormone that modulates a number of metabolic processes, including **glucose** regulation.

Clearly, one skilled in the art would have assumed the method of the copending application would inherently perform the instant mechanism of the present application.

Claims 13. 15-18, 25, 27 and 28 are not allowed.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 13, 15-18, 25, 27, 28 and 31 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This is a written description rejection.

A lack of adequate written description issue arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process. See, e.g., Fujikawa v. Wattanasin, 93 F.3d 1559, 1571, 39 USPQ2d 1895, 1905 (Fed. Cir. 1996) (a "laundry list" disclosure of every possible moiety does not constitute a written description of every species in a genus because it would not "reasonably lead" those skilled in the art to any particular species); In re Ruschig, 379 F.2d 990, 995, 154 USPQ 118, 123 (CCPA 1967).

An applicant may also show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics which provide evidence that applicant was in possession of the claimed invention, i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.

In particular, the specification as original filed fails to provide sufficient written bases of any of the agents demonstrating wherein possession of use of the broad term HMG-CoA reductase inhibitor(s). The genus has not being appropriately defined. The mere fact that Applicant may have discovered one specific HMG-CoA reductase inhibitor to be effective to enhance glucose uptake in animal cells is not sufficient to claim the entire genus.

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. See Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406.

A "representative number of species" means that the species, which are adequately described, are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. The disclosure of only one species encompassed within a genus adequately describes a claim directed to that genus only if the disclosure "indicates that the patentee has invented species sufficient to constitute the gen[us]."

Claims 13, 15-18, 25, 27, 28 and 31 are not allowed.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 13, 15-18, 25, 27, 28 and 31 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 13, 15-18, 25, 27, 28 and 31 described compounds that are HMG-CoA reductase inhibitors. The instant claims cover all compounds having the pharmaceutical property of being a HMG-CoA reductase inhibitor to enhance glucose uptake in warm-blooded animal cells. Describing a compound by its functions will not substitute for written description of the structure of the compound. The invention should be described in such a way as to described what the invention is, not what the invention does. Describing the function of a compound fails to distinguish the compound from other molecules or agents that can perform the same functions.

Undue experimentation is a conclusion reaches by weighing the noted factual considerations set forth below as seen in In re Wands, 858 F. 2d 731, 737, 8 USPQ2d 1400, 1401 (Fed. Cir. 1988). A conclusion of lack of enablement means that, based on the evidence regarding a fair evaluation of an appropriate combination of the factors below, the specification, at the time the application was filed, would not have taught

one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation.

The factors include:

1) the quantity of experimentation necessary

2) the amount of direction or guidance provided

3) the presence or absence of working examples

4) the nature of the invention

5) the state of the art

6) the relative skill of those in the art

7) the predictability of the art and

8) the breadth of the claims

The instant specification fails to provide guidance that would allow the skilled artisan background sufficient to practice that instant invention without resorting to undue experimentation in view of further discussion below.

The nature of the invention, state of the prior art, relative skill of those in the art and the predictability of the art

Claims 13, 15-18, 25, 27 and 31 are directed to compounds that are HMG-CoA reductase inhibitors that are used to enhance glucose uptake into warm-blooded animal cells. The instant claims cover all compounds having pharmaceutical property of being known as a compound (HMG-CoA reductase inhibitor) to enhance glucose uptake into warm-blooded animal cells. Although claims 15, 17, 27 and 28 lists specific examples of compounds which are alleged to have the property to enhance

glucose uptake into warm-blooded animal cells, and claims 13, 15 and 16 are directed to a variety of compounds with the functional description of being known as a compound which is alleged to have the property to enhance glucose uptake into warm-blooded animal cells.

The prior art, Drug Digest.Org, teaches HMG-CoA reductase inhibitors as statins. Note the statin drug, Cerivastatin, is withdrawn from the market (Baycol).

The instant claims are very broad. For instance, claims 13, 15 and 16 are to a plethora of compounds of as described by the functional properties as being known to treat neurological disorders.

The relative skill of those in the art is generally that of a Ph.D. or M.D.

One skilled in the art would not predict from the instant disclosure which compounds would fall under the umbrella of functional description of being known as broadly as a HMG-CoA reductase inhibitor. In fact, the courts have made a distinction between mechanical elements function the same in different circumstances, yielding predictable results, chemical and biological compounds often react unpredictably under different circumstances.

The breadth of the claims

The claims are very broad and inclusive to all HMG-CoA reductase inhibitors, including the withdrawn cerivastatin, are used to enhance glucose uptake into warm-blooded animal cells.

The amount of direction or guidance provided and the presence or absence of working examples

The working examples are limited to the administration of pravastatin only.

No examples showing the combination of two or more HMG-CoA reductase inhibitors together.

No examples showing how cerivastatin (withdrawn from the market) is used to enhance glucose uptake into warm-blooded animal cells.

The quantity of experimentation necessary

Applicants have failed to provide guidance as to how the skilled artisan would be able to extrapolate from the disclosure and examples provided to make and possibly use the claimed invention. The amount of guidance or direction needed to enable the invention is inversely related to the degree of predictability in the art. Thus, although a single embodiment may provide broad enablement in cases involving predictable factors, such as mechanical or electrical elements, in cases involving unpredictable factors, such as most chemical reactions and physiological activity, more teaching or guidance is required. (In re Fischer, 427 F. 2d 839, 166 USPQ 24; Ex Parte Hitzeman, 9 USPQ 2d 1823).

The quantity of experimentation needed to be performed by one skilled in the art is yet another factor involved in the determining whether "undue experimentation" is required to make and use the instant invention. The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or of the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. For these reasons, one of ordinary skill in the art would be burdened with

undue "painstaking experimentation study" to determine all the compounds or agents that are broadly known to possess the property of enhancing glucose uptake into warm-blooded animal cells described in this specification. In view of the information set forth supra, the instant disclosure is not seen to be sufficient to describe the use of any compound , which is regarded as the functional description of a compound (HMG-CoA reductase inhibitor) for enhancing glucose uptake into warm-blooded animal cells.

Therefore, undue experimentation would be required to practice the invention as it is claimed in its current scope.

Claims 13, 15-18, 25, 27, 28 and 31 are not allowed.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 13, 15-18, 25, 27 and 28 are rejected under 35 U.S.C. 102(b) as being anticipated by Paolisso et al., "Simvastatin reduces plasma lipid levels and improves insulin action in elderly, non-insulin dependent diabetes", European Journal of Clinical Pharmacology, Vol. 40, No. 1, pp. 27-31; Cingözbay et al., Current Diabetes Reports of PTO-1449; Freeman et al., Circulation of PTO-1449; and Mangaloglu et al., Metabolism of PTO-1449.

Paolisso et al. teach the administration of simvastatin in elderly non-insulin dependent diabetes patients exert beneficial effects both on lipid and glucose metabolism in various cells (See the abstract).

Cingözbay et al. teach the effects of fluvastatin in the treatment of insulin sensivity in patients with hyperlipidaemia. Note the reference teaches the administration of fluvastatin increased insulin sensitivity (insulin resistance), wherein insulin resistance reduces glucose uptake in cells (See the abstract).

Freeman et al. teach the administration of pravastatin may significantly influence selective tissue perfusion and thereby beneficially affect glucose and insulin transport (see page 7, section four, stating with the word "Finally").

Mangaloglu et al. teach a treatment with atorvastatin ameliorates hepatic very-low-density lipoprotein in animal model of insulin resistance. Note the reference teaches atorvastatin enhance hepatic insulin sensitivity (insulin resistance) in the instant abstract.

Clearly, each one of the four references teaches a HMG-CoA reductase inhibitor is used to treat insulin sensitivity (same as insulin resistance that reduces glucose uptake) in warm-blooded animal cells.

The four references, individually, teaches every element of the instant invention.

Claims 13, 15-18, 25, 27 and 28 are not allowed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 31 is rejected under 35 U.S.C. 103(a) as being unpatentable over Paolisso et al., "Simvastatin reduces plasma lipid levels and improves insulin action in elderly, non-insulin dependent diabetes", European Journal of Clinical Pharmacology, Vol. 40,

No. 1, pp. 27-31; Cingözbay et al., Current Diabetes Reports of PTO-1449; Freeman et al., Circulation of PTO-1449; and Mangaloglu et al., Metabolism of PTO-1449 in view of Weiner et al. (5,643,868).

The four primary references were discussed above supra for the administration of various HMG-CoA reductase inhibitors used to increase or to enhance glucose uptake in warm-blooded animal cells.

The instant invention differs from the cited reference in that the cited reference does not teach the addition of insulin. However, the secondary reference, Weiner et al., teaches administration of insulin to animals suffering diabetes. Note the administration of insulin does not decrease blood sugar (glucose) in pancreatic beta cells in a mammal (an animal).

Clearly, one skilled in the art would have assumed the combination of two individual agents well-known to increase blood sugar (glucose) in cells into a single composition would give an additive effect in the absence of evidence to the contrary.

Claim 31 is not allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kevin E. Weddington whose telephone number is (571)272-0587. The examiner can normally be reached on 12:30 pm-9:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571)272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Kevin E. Weddington
Primary Examiner
Art Unit 1614

K. Weddington
August 3, 2007